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Integrative multi-omics profiling for resectable hepatocellular carcinoma uncovers clinically available serum biomarkers to predict microvascular invasion

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Introduction : Microvascular invasion (MVI) is a well-known prognostic factor to predict cancer relapse after curative resection of resectable hepatocellular carcinoma (HCC). It is mandatory to uncover clinically available serum biomarkers to predict the MVI feature at the initial diagnosis of HCC.

Methods : Using gene expression profiling for resected human HCC (Discovery cohort, n=240), we identified transcriptomic signature predicting the MVI feature. Repeated validation for the MVI signature performed using the Bayesian covariate compound predictor method at the multiple independent cohorts (Six Validation cohorts, n=1,263). Serum biomarker dataset from the patients of TCGA-LIHC samples correlated with the MVI signature.

Results : The MVI signature with 1028 genes was identified from robust statistical testing from the discovery cohort, and robust validation for the prediction performance of the MVI signature showed significant accuracy in the validation cohort (AUC=0.865, p<0.01). Multi-omics analysis revealed aggressive tumor biology associated with the MVI signature regarding FOXM1, CD24, and MYC downstream pathways. A diagnostic panel from integrating significant serum biomarkers to predict MVI was identified from stepwise regression (p<0.001). Comprehensive analysis of drug-sensitivity for the MVI signature was performed by integrative insilico prediction methods using the dataset from Cancer Dependency Map project.

Conclusions : Integrative multi-omics profiling for resectable HCC uncovers clinically available serum biomarkers to predict MVI without a surgical specimen. A novel combination of serum biomarkers shows high performance in sorting out the tumor with aggressive tumor biology. Precision strategy to discover resectable tumors beneficial from surgical resection can be established from consecutive clinical trials based on this translational study.

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